

Remarks

Claims 1-8 are pending in the application and claims 21-22 are withdrawn from consideration. Applicants hereby cancel claims 21-22 upon Examiner's request. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application. Claims 1 and 2 have been amended, and new claims 23-34 have been added. No new matter has been added. Certain minor typographical errors have been corrected by the amendments. Support for the amendments may be found throughout the specification, including the claims as originally filed. For example, support for amended claims 1 and 2 may be found in the specification on page 1, in Figure 5, its legend on pages 14-15, and on page 61. Exemplary support for certain of the new claims may be found as follows:

Claims 23-27: page 5, pages 22-23, page 25, and page 61.

Claims 30-32: page 35, page 47.

Claims 33-34: pages 34-35, page 47.

Amendment of claims should in no way be construed to narrow their scope or as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

**Rejection of claims 1-3 and 5-8 under 35 U.S.C. § 112, first paragraph**

The Examiner has rejected claims 1-3 and 5-8 under 35 U.S.C. § 112, first paragraph as allegedly unenabled because the specification, while being enabling for the crystal of *Thermus aquaticus* bacterial core RNA polymerase, does not provide enablement for a crystal of any other bacterial or other source core RNA polymerase suitable for the same resolution determination. The Examiner urged that the only crystal demonstrated to enable the required X-ray diffraction is the *Thermus aquaticus* bacterial core RNA polymerase crystal, and that although there is general guidance regarding preparation of core RNA polymerase crystals from other bacterial sources, there is no clear teaching on how to arrive at crystals with the required X-ray quality.

Applicants respectfully point the Examiner's attention to MPEP § 2164.01, which cites United States v. Electronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988): "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." Further, Application also respectfully point the Examiner's attention to MPEP § 2164.02, which states in relevant part: "[t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors."

Therefore, Applicants respectfully submit that the disclosed preparations of high quality crystals of *Thermus aquaticus* bacterial core RNA polymerase as well as several heavy metal atom derivatives thereof, are sufficient to enable the preparation of other RNA polymerase crystals without undue experimentation when coupled with the general guidance provided in the specification as well as techniques known in the art for the preparation of high quality crystals. Such preparation may, for example, entail screening a fairly large number of conditions which are variations on the conditions disclosed in the instant specification. As noted in Ex parte Forman, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) and In re Brandstadter, 484 F.2d 1395, 1407, 179 USPQ 286,294-295 (CCPA 1973), a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance. Screening a matrix of iterative variations on a condition known to afford a crystal is routine in the crystallography art. Therefore, Applicants respectfully urge that the

disclosure in the specification is sufficient to allow one of skill in the art to practice the claimed invention without undue experimentation, and request withdrawal of the rejection.

**Rejection of claim 6 under 35 U.S.C. § 112, first paragraph**

The Examiner has rejected claim 6 under 35 U.S.C. § 112, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application had possession of the claimed invention because the specification does not demonstrate a crystal of a core RNA polymerase having a  $\omega$  subunit. Applicants respectfully point out that an embodiment of the *Thermus aquaticus* bacterial core RNA polymerase disclosed in the specification contains a  $\omega$  subunit, as noted at pages 48 in lines 26-27, page 53 in lines 24-29, and page 54 in Table 2 and lines 1-2. Therefore, Applicants respectfully request the withdrawal of the rejection.

**Rejection of claims 1, and 5-7 under 35 U.S.C. § 102(b) over Jeruzalmi, et al**

The Examiner has rejected claims 1, and 5-7 under 35 U.S.C. § 102(b) as anticipated by Jeruzalmi, et al. (J. Mol. Biol. 274 (5), 748-756, 1997), which teaches crystals of T7 bacteriophage RNA polymerase that diffract to high resolution. Applicants have amended claim 1 to recite “core RNA polymerase (RNAP) from a eukaryote or prokaryote”. Thus, because Jeruzalmi teaches the preparation of a crystal of a T7 bacteriophage RNA polymerase, which is a viral polymerase rather than a prokaryotic or eukaryotic RNA polymerase as required by amended claim 1, the rejection has been rendered moot. Applications respectfully request withdrawal of the present rejection and reconsideration of the amended claims.

**Rejection of claims 1-3, and 5-7 under 35 U.S.C. § 102(b) over Polyakov, et al**

The Examiner has rejected claims 1-3, and 5-7 under 35 U.S.C. § 102(b) as anticipated by Polyakov, et al. (Cell, 83, 365-373, 1995), which allegedly teaches crystals of bacterial RNA polymerase having  $\alpha\alpha\beta\beta'$  subunits. Examiner asserts, citing In re Pearson (494 F.2d 1399, 181 USPQ 641 (CCPA 1974)) that the claimed limitation regarding intended use for determination of atomic coordinates is an intended use limitation, which does not impart patentability to

product claims where the product is otherwise anticipated by the prior art. Applicants respectfully point out that In re Pearson held that intended use limitations could be used to distinguish a composition from the prior art so long as “such terms … define, indirectly at least, some characteristic not found in the old composition.” (In re Pearson, at 1403) Applicants assert that the present limitation “effectively diffracts X-rays for the determination of the atomic coordinates to a resolution of better than 3.5 Angstroms” is such a limitation in that it defines a characteristic not found in the Polyakov crystal – the ability of the presently claimed crystals to diffract X-rays for the determination of atomic coordinates to a resolution of better than 3.5 Angstroms. The crystal of Polyakov, et al. diffracted electrons to a much lower resolution of 23 Angstroms (see, e.g. the abstract and page 365, 2<sup>nd</sup> column, 1<sup>st</sup> full paragraph) in only two dimensions (see, e.g. page 366, first paragraph.) The crystal of Polyakov, et al was prepared on positively charged lipid layers, a technique for preparing *two-dimensional crystals* suitable for electron microscopy, rather than a technique for preparing three-dimensional crystals suitable for high-resolution structure determination by x-ray crystallography. The two-dimensional crystals of Polyakov, et al., could not be used to determine at high resolution a set of three-dimensional atomic coordinates using x-ray crystallography. Thus, the present limitation can be used to distinguish the presently claimed crystal from the crystal of Polyakov, et al because it defines a characteristic not found in the Polyakov, et al crystal, that is, suitability for use in the determination of three-dimensional atomic coordinates by x-ray crystallography. Applicants have amended claims 1 and 7 to clarify this distinction. Hence, Applicants respectfully request withdrawal of the present rejection.

**Rejection of claims 1, 2, 5, and 7 under 35 U.S.C. § 102(a) over Darst, et al**

The Examiner has rejected claims 1, 2, 5 and 7 under 35 U.S.C. § 102(a) as anticipated by Darst, et al. (J. Struct Biol., 124, 115-122, 1998), which teaches allegedly teaches crystals of *E. coli* RNA polymerase having  $\alpha\alpha\beta\beta'$  subunits. Examiner also cites In re Pearson (494 F.2d 1399, 181 USPQ 641 (CCPA 1974)) and asserts the alleged intended use limitation “effectively diffracts X-rays for the determination of the atomic coordinates to a resolution of better than 3.5 Angstroms” does not serve to distinguish the claimed crystals from those of Darst, et al. Applicants respectfully reiterate that In re Pearson held that intended use limitations could be used to distinguish a composition from the prior art so long as “such terms must define,

indirectly at least, some characteristic not found in the old composition.” (In re Pearson, at 1403) Applicants assert that the present limitation defines a characteristic not found in the Darst crystal – the ability of the presently claimed crystals to diffract X-rays to a resolution of better than 3.5 Angstroms. Darst, et al., specifically states on page 120 that, although the Darst, et al. crystals were sufficient for analysis of structure using electron microscopy, “we lack 3D crystals of *E. coli* RNAP that are suitable for x-ray analysis. . .” Thus, the present limitation can be used to distinguish the presently claimed crystal from the crystal of Darst, et al because it defines a characteristic not found in the Darst, et al crystal, that is, suitability for use in the determination of three-dimensional atomic coordinates by x-ray crystallography. Applicants have amended claims 1 and 7 to clarify this distinction. Hence, Applicants respectfully request withdrawal of the present rejection.

### Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-832-1000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this application be charged to Deposit Account, No. 06-1448.

Respectfully submitted,

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